

Outcomes of Endovascular Treatment for Intracranial Mycotic Aneurysms: A Retrospective Data Analysis of a Tertiary Center

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Abstract

Purpose: The aim of this study was to investigate the clinical and imaging features of intracranial mycotic aneurysms (MAs) in addition to endovascular treatment (EVT) results with different techniques.

Methods: Patients who underwent EVT for MAs between 2007 and 2021 were included in this retrospective study. All patients underwent at least one of the cranial cross-sectional imaging modalities [computed tomography (CT) or magnetic resonance imaging (MRI)] before EVT to demonstrate the presence of an abscess or intracranial hemorrhage. Digital subtraction angiography (DSA) examination was used to assess different MA characteristics. The primary goal of EVT in all cases was to prevent the filling of the aneurysm sac. In a case where direct access to the aneurysm could not be achieved, only the parent artery was occluded by the injection of an embolizing agent. After EVT, follow-up DSA at the sixth month and MRI and CT angiography examinations at the first year were obtained.

Results: Twelve patients with a total of 20 MAs were included, with a mean age of 32.83 (range 12-66). All of the MAs were located distally in the intracranial circulation. At the admission time, 5 (41.66%) of the patients had intracranial hematoma. Sixteen out of 20 aneurysms were treated endovascularly. Aneurysm sac embolization and parent artery occlusion were carried out in 12 (75%) of the 16 treated aneurysms. Newly developed aneurysms or aneurysms with residual filling were not detected in the sixth-month DSA.

Conclusion: Endovascular treatment can be safe and effective in most cases of MA. Early diagnosis and individualized treatment are key to the success of treatment.

Keywords: Digital subtraction angiography, endovascular treatment, intracranial mycotic aneurysm

Introduction

Intracranial mycotic aneurysms (MA) are rare neurovascular lesions that account for 0.7%-5.4% of all cerebral aneurysms.¹ These aneurysms, also known as intracranial infectious aneurysms, develop as a result of microbial infection and necrosis in the vessel wall as a result of septic embolism from a proximal source of infection. Although bacterial endocarditis is the most common underlying risk factor, fungal infections may also play a role in the etiology of MAs.^{2,3} The infectious organism must be detected in a blood or cerebrospinal fluid culture for a conclusive diagnosis. Nevertheless, in many patients with the effect of partial antimicrobial treatment, it is challenging to isolate the causative infectious pathogens.⁴

Digital subtraction angiography (DSA) is the gold standard method in the diagnosis of intracranial MA, and some distinctive

angiographic features have been defined for these aneurysms, such as distal location on middle cerebral artery (MCA) (less frequently on posterior cerebral artery (PCA) branches), irregular contours, and multiplicity. These lesions are prone to rupture and are therefore associated with a high mortality rate of up to 80%.^{2,5} Moreover, intracranial MAs are dynamic lesions with the potential for rapid change. Therefore, close angiographic follow-up is required in cases treated with antibiotics.⁶

There is no widely accepted standard management protocol addressing the treatment of this uncommon type of cerebral aneurysm due to the variability in their course and clinical presentations as well as the dearth of population-based epidemiological data.⁴ The treatment of cases with MA is tailored on a patient basis in light of the patient's clinical status, clinical presentation, relation of aneurysm to eloquent parent arteries, morphology of the aneurysm, and stability status of aneurysm.^{1,7} Treatment options include antibiotics, surgery, and endovascular intervention. Therefore, treatment requires a multidisciplinary approach. Neuroendovascular therapy has become a first-line intervention in the majority of patients thanks to advances in the endovascular field, especially in the last decade.⁸

In this study, we aimed to investigate the clinical and imaging features of patients with intracranial MA in addition to the endovascular treatment (EVT) results with different techniques.

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Methods

Patients

This retrospective study was approved by İstanbul University Cerrahpaşa, Cerrahpaşa Faculty of Medicine ethics committee (Approval No: 660643, Date: April 4, 2023) and carried out according to the requirements of the Declaration of Helsinki. Written informed consent was obtained from all participants of this study.

A total of 12 patients who underwent EVT for MAs, both ruptured and unruptured, in our interventional neuroradiology department between 2007 and 2021 were included in this retrospective study. Patients with intracerebral hemorrhage but lacking evidence of infected aneurysms and patients without control DSA examination were excluded from the study, considering that it would be inadequate to show accurate treatment results.

Diagnostic Evaluation

The diagnosis of MA was based on the presence of an aneurysm located distal to the intracranial arterial structures in DSA examination, along with the presence of underlying infectious disease (particularly infective endocarditis), clinical predisposing factors, and/or positive blood / cerebrospinal fluid (CSF) culture and echocardiographic findings. Two patients who received empirical antibiotic therapy and had negative blood/CSF cultures and no evidence of vegetation on echocardiography were accepted as having an infectious source of illness due to additional clinical findings like fever, leukocytosis, a high erythrocyte sedimentation rate, and high C-reactive protein levels in addition to distal aneurysms in the DSA examination.

Distal intracranial aneurysms, proximal intracranial aneurysms with an atypical morphology unrelated to branching points, which are more common with noninfectious aneurysms, and aneurysms developed on the basis of infective endocarditis or systemic infection that were negative on initial DSA examinations but emerged in subsequent DSA examinations are DSA features that are consistent with infectious etiology.^{1,4,5}

All patients underwent at least one of the cranial cross-sectional imaging modalities [cranial computed tomography (CT) or magnetic resonance imaging (MRI)] before EVT to demonstrate the presence of an abscess or intracranial hemorrhage. The DSA examination was used as the mainstay radiological modality to assess the localization, size, and morphology of the aneurysm and to definitively diagnose the source of bleeding, if any.

Treatment

Patients with proven or suspected MAs were initially treated with the proper antibiotics prescribed by physicians from Infectious Diseases and Clinical Microbiology, and aneurysms were subsequently secured by endovascular therapy. All endovascular procedures were carried out by at least 2 senior neuroradiologists (C.I., N.K., and O.K.) on Philips Integris Allura and Allura Xper FD 20/20 Biplane Angiography (Philips Medical Systems, Netherlands). Unilateral femoral access was used under general anesthesia after obtaining informed consent.

Following the placement of an appropriate guiding catheter, a microcatheter (standard for coil or flow directed for liquid embolic agents) with an appropriate microguidewire was used to provide access to the aneurysm site. In distally located aneurysms, the microcatheter was advanced as close as possible to, and ideally inside, the aneurysm. Detachable coils, or liquid embolic agents (Glue, Covidien, Irvine, CA, USA), were delivered under fluoroscopic control into the aneurysm lumen and/or parent artery. Although the primary goal of EVT in all cases

in our series was to prevent the filling of the aneurysm sac, there were cases where the parent artery had to be closed. In a case where direct access to the aneurysm could not be achieved, only the parent artery was occluded by the injection of an embolizing agent as close to the aneurysm as possible. In cases treated with embolizing agents, a 50 : 50 mixture of lipiodol and N-butylcyanoacrylate (NBCA) was used and slowly injected. Before the parent artery occlusion, a balloon occlusion test was performed in 3 cases in which MAs were located proximal to the MCA M3 segment, whereas the Wada test was not used in any treatment procedure. In 1 patient, cerebral hemorrhagic complications necessitated a craniotomy for hematoma evacuation and ventricular drainage.

Follow-Up and Treatment Outcome

After the treatment, DSA examinations at the sixth month and control MRI and CT angiography examinations at the first year were obtained. Postsurgical control examinations were performed with CT and CT angiography in the patient who underwent hematoma evacuation due to intraparenchymal hematoma.

Treatment success was defined as resolution of the aneurysm on follow-up imaging and absence of rebleeding and/or procedural complications. The modified Rankin Scale was used to evaluate the clinical outcomes.

Statistical Analysis

Statistical analyses were performed using The Statistical Package for Social Sciences version 23.0 software (IBM Corp.; Armonk, NY, USA). After the research data was digitized, frequency and percentage values were calculated for categorical variables, and mean and standard deviation values were calculated for continuous variables.

Results

Twelve patients with a total of 20 MAs were included in the study. The mean age of the patients was 32.83 (\pm 12.99, ranging between 12 and 66), and 8 (66.66%) patients were female. The diagnosis of intracranial aneurysm was confirmed by DSA in all patients. All of the aneurysms were located distally in the intracranial circulation. Fifteen aneurysms (75%) were in the anterior circulation; the remaining 5 (25%) aneurysms were located in the posterior circulation. Based on the aneurysmal morphology, localization features, and clinical findings mentioned above, patients were diagnosed with MA.

Ten (83.33%) out of 12 patients exhibited valve vegetations that were indicative of endocarditis. The blood cultures were detected to be positive for infectious agents in 7 (58.33%) patients. Blood culture and cardiac ultrasonography results were found to be negative under empirical antibiotic therapy in 2 (16.67%) patients; however, the intracranial aneurysms were considered to be of infectious origin due to findings suggestive of an infectious etiology, such as leukocytosis, high erythrocyte sedimentation rate, high C-reactive protein levels, and fever.

In the cross-sectional cranial imaging examinations (cranial CT or MRI) performed at the time of admission, 5 (41.66%) of the patients had intracranial hematoma, while no findings regarding intracranial hemorrhage were found in 7 (58.33%) patients. Intraparenchymal hematoma, subarachnoid hemorrhage, and subdural hemorrhage were detected in 4 (80%), 1 (20%), and 1 (20%) of the cases with ruptured MAs, respectively. Two (40%) of the patients had experienced simultaneously different types of intracranial hemorrhage patterns. Whereas headache and neurological deficits are the most frequently reported major complaints

in patients with ruptured MAs, headache and fever are the most predominant symptoms in those with unruptured MAs.

Endovascular treatment under antibiotics was aimed as soon as possible after the diagnosis of 20 MAs, 5 of which ruptured. The patients who were detected to have ruptured aneurysms were treated on the same day of diagnosis, and the patients with unruptured MAs were treated endovascularly within a week after diagnosis. A total of 16 MAs were treated endovascularly. In one of the patients (patient 8), 3 aneurysms with fusiform features located distally in the left MCA region were not treated endovascularly, and the patient was administered antibiotherapy. In one of the remaining aneurysms, spontaneous occlusion was observed in the angiograms (patient 1) during the EVT session (Figure 1). Aneurysm sac embolization and parent artery occlusion (PAO) were carried out in 12 (75%) of 16 treated aneurysms (Figure 2).

The remaining 4 aneurysms were treated successfully with intrasaccular aneurysm occlusion using coils due to their wide aneurysmal sacs (Figure 3). In one of the patients, the abscess formation, which was observed around the aneurysm sac at the time

of admission, showed total regression after antibiotherapy and EVT (Table 1).

Craniotomy was performed for hematoma evacuation due to the mass effect in 2 patients prior to treatment. In total, 3 patients underwent cardiac surgery within 1 month following EVT. Neither newly developed aneurysms nor aneurysms with residual filling were detected in the sixth-month control DSA examination in any of the patients. Although no EVT-related mortality was observed during the follow-up period, 2 of the patients died within 2 years as a result of cardiorespiratory complications.

Discussion

Although MAs may present with different clinical scenarios, they most commonly occur following aneurysm rupture.⁴ In our study group, 5 (41.66%) of our 12 patients presented with signs of intracranial hemorrhage. Of the patients who presented with intracranial hemorrhage, 80% (n = 4) were found to have intraparenchymal hemorrhage, 20% (n = 1) to have subarachnoid hemorrhage, and 20% (n = 1) to have subdural hemorrhage. As has been demonstrated by different studies in the literature, the tendency for

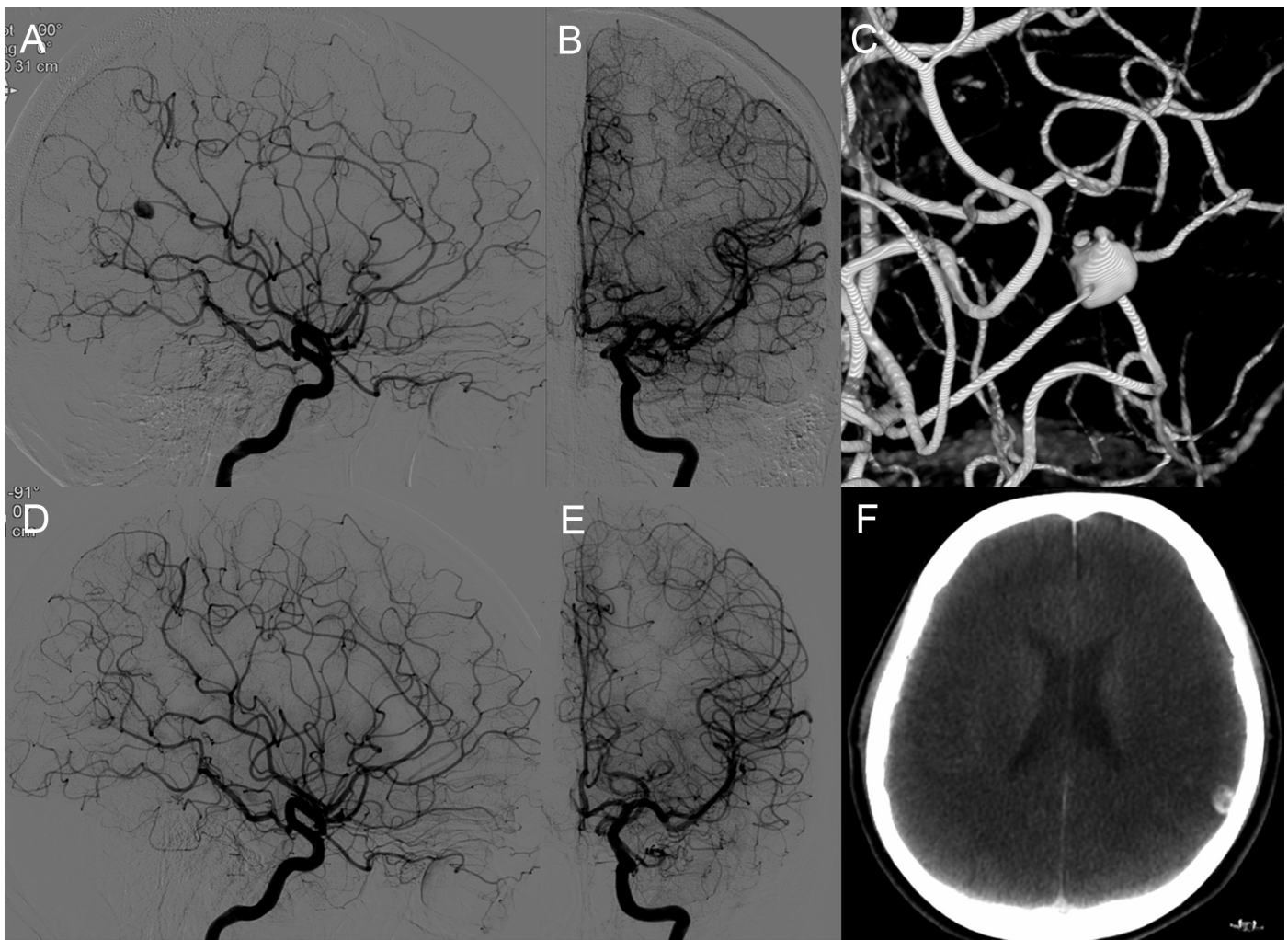


Figure 1. (A, B) The mycotic aneurysm, that was detected on left MCA posterior parietal artery distal branch in an 18-year-old patient, was shown in lateral and Anteroposterior (AP) digital subtraction angiographic views obtained via left internal carotid artery (ICA) injection. (C) 3D reconstruction image of the mycotic aneurysm. (D) Lateral and (E) AP digital subtraction angiographic views obtained at the beginning of the treatment session revealed spontaneous occlusion of the aneurysm. (F) Control cranial computed tomography following the spontaneous occlusion of the aneurysm showed the hyperdense nodular lesion (thrombosed aneurysm) on the left parietal region.

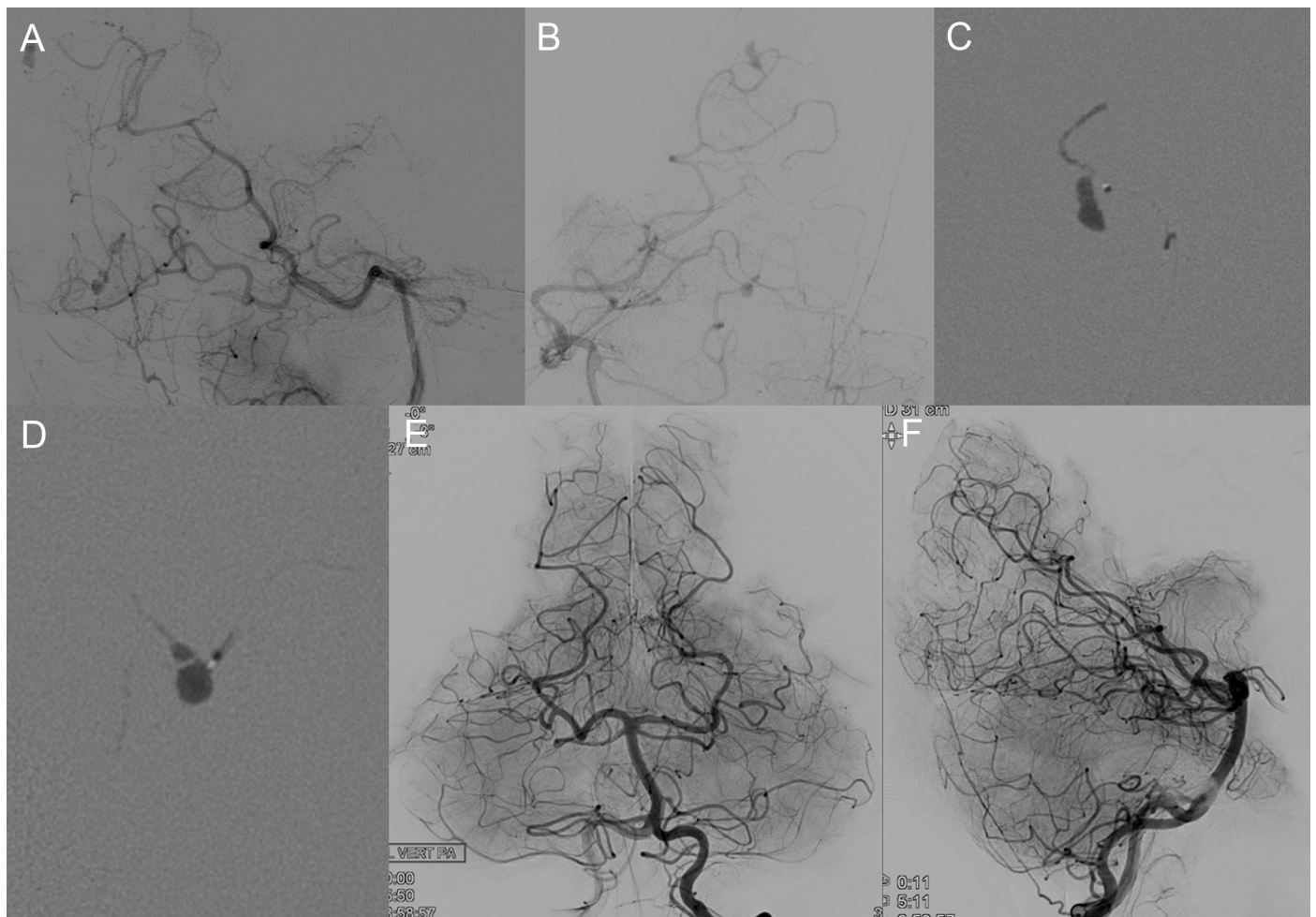


Figure 2. A 56-year-old male patient with known diagnosis of endocarditis presenting with headache. (A) Lateral and (B) oblique views of left vertebral artery injection showed 2 mycotic aneurysms in the right distal posterior cerebral artery. (C) and (D) demonstrate the injection of 50:50 mixture of lipiodol and N-butyl-cyanoacrylate in order to obliterate the aneurysm sac and its parent artery. Left vertebral artery angiogram (E) AP and (F) lateral views showed total occlusion of both mycotic aneurysms at 6 months postoperatively.



Figure 3. (A) A 35-year-old male patient presented with a right frontal intraparenchymal hematoma, that was shown in cranial CT. (B) Right internal carotid artery lateral angiogram reveals a mycotic aneurysm at the A4 segment of right anterior cerebral artery (arrow). (C) The image reveals 3D reconstruction of the aneurysm. (D) The roadmap image showing the tip of microcatheter just inside the aneurysm sac during the coil embolization. (E) Final angiogram after 6 months postoperatively showing total occlusion of the aneurysm sac following embolization with coils (arrow).

intraparenchymal hemorrhage was found to be higher in patients with intracranial MAs compared to noninfective aneurysms.⁴ In our study group, the mean diameter of aneurysms presenting with intracranial hemorrhage was found to be 3.8 mm, while the mean diameter of aneurysms that did not present with hemorrhage was 8.7 mm. As shown in our study and several studies in the

literature, size does not seem to be a reliable predictor of rupture for intracranial MAs.^{4,5}

Considering the strong relationship between endocarditis and intracranial MA, cerebrovascular imaging may be beneficial in all patients who develop neurological deficits under the diagnosis of bacterial endocarditis.^{4,9} Moreover, in a patient presenting with

Table 1. Clinical and angiographic characteristics of the study group

	Age	Gender	Presentation	Aneurysm Location	Number of Aneurysms	Aneurysm Rupture	Treatment	Treatment Material	Outcome (90 days mRs)
Patient 1	18	F	Headache, fever	L MCA M4 saccular	1	–	Spontaneous Occlusion	-	1
Patient 2	15	F	Headache, fever	R MCA M3 saccular	1	–	PAO + Aneurysm Sac Occlusion	Glue	1
Patient 3	54	M	Headache, fever	R MCA M4-5	1	–	PAO + Aneurysm Sac Occlusion	Glue	1
Patient 4	32	F	Subdural hematoma (15 mm in width) Cortical abscess 1.5 × 1 cm	R MCA M3, R MCA M4, R PCA P3	3	+	PAO + Aneurysm Sac Occlusion	Glue + Coils	2
Patient 5	45	F	IPH 5 × 4 cm	L MCA M2-M3	1	+	PAO + Aneurysm Sac Occlusion	Glue	4
Patient 6	30	M	Neurological deficit related to the infarcted area in MCA territory	L MCA M2	1	–	PAO + Aneurysm Sac Occlusion	Glue	2
Patient 7	66	F	Headache, fever	R MCA M3-M4	1	–	Aneurysm Sac Occlusion	Coils	1
Patient 8	56	M	Headache, fever	L MCA M3-M4, L MCA M4-M5, R PCA P2, R PCA P3	6	–	Aneurysm Sac Occlusion, PAO + Aneurysm Sac Occlusion	Glue	1
Patient 9	15	F	IPH 5 × 4.5 cm	L MCA M4-M5	1	+	PAO + Aneurysm Sac Occlusion	Glue	3
Patient 10	16	M	Neurological deficit related to the infarcted area in MCA territory	L MCA M2-M3	1	–	Aneurysm Sac Occlusion	Coils	2
Patient 11	35	F	IPH 3 × 2.5 cm	R PCA P2-P3, R ACA A4	2	+	Aneurysm Sac Occlusion, PAO + Aneurysm Sac Occlusion	Glue + Coils	2
Patient 12	12	F	SAH, IPH 3 × 2 cm	L PCA P3	1	+	Aneurysm Sac Occlusion	Coils	2

F, female; IPH, intraparenchymal hemorrhage; M, male; MCA, middle cerebral artery; mRS, modified Rankin scale; PAO, parent artery occlusion; PCA, posterior cerebral artery; SAH, subarachnoid hemorrhage.

SAH due to their young age, presence of fever, and detection of more than 1 distally located aneurysm, the diagnosis of MA should be considered, and underlying infectious etiologies such as bacterial endocarditis should be investigated thoroughly.⁴ Nevertheless, in a significant portion of the patients, blood and CSF cultures may be detected as negative as a result of empirical antibiotic therapy, failure to thoroughly investigate potential pathogens, or the development of MAs in a weakened vessel wall following the clearance of the underlying pathogen.^{8,10} For instance, 2 patients who received empirical antibiotic therapy and had negative blood/CSF cultures and no evidence of vegetation on echocardiography were accepted as having MA due to clinical findings indicating infectious etiology in our study.

Due to the small size of MAs, DSA is the gold standard radiological modality in the identification of these aneurysms when compared with CT angiography or MR angiography, which have approximately 40% sensitivity in the detection of MAs.^{4,11} Classical angiographic hallmarks of MAs include multiplicity, distal location,

fusiform shape, and change in the size or appearance of a new aneurysm on the follow-up angiogram.⁴ In our study, all but one of the MAs located in the MCA were distal to the M2 segment. In addition, all of the 5 MAs located in the PCA were distal to the P1 segment. Three patients (25%) in the study group had multiple aneurysms.

The rapid and dynamic changes in the vessel wall associated with MAs may explain the higher bleeding rate when compared with noninfectious intracranial aneurysms. This may be supported by the finding that rapid changes in MAs on serial imaging herald subsequent bleeding or rupture.¹² The time between the onset of infective endocarditis and the rupture of MAs can vary between 2 and 5 weeks.¹³ In immunocompromised individuals, MAs are larger and tend to grow faster than in immunocompetent ones.¹⁴

According to a systematic review by Alawieh et al, the preference for medical management and open surgical procedures has decreased over the past 2 decades with an increase in the utilization of endovascular therapy. There was a substantial increase

in the use of endovascular approaches in 2007-2017 (45.1%) compared with 1997-2007 (16.8%) ($P < .05$).⁸ Besides, a significantly higher rate of treatment success was also observed with open surgical and endovascular treatment compared with medical therapy ($P < .001$). Nevertheless, in the restricted analysis regarding the studies published between 2007 and 2017, only EVT showed a significant reduction in mortality compared with medical management.⁸

In the aforementioned systematic review, it was also stated that the rates of complications following surgery or EVT did not differ significantly (9.1% vs. 7.6%, $P > .05$) (8). Intra-procedural hemorrhage, congestive heart failure, and ischemic stroke secondary to vessel sacrifice were among the reported complications related to open surgical procedures. Complications following EVT included neurological deficit following parent vessel occlusion (most frequent), intraparenchymal hemorrhage, cardiac arrest, vessel perforation, and failure of complete occlusion with residual filling of the aneurysm.⁸ The ability to perform a balloon occlusion test in conjunction with endovascular procedures to assess the risk of ischemic consequences provides significant benefit.^{9,12} Since all MAs treated in our study group were located in the distal circulation and balloon test occlusion was performed only for 3 patients with aneurysms located proximal to MCA M3 segment before the treatment, deficits due to parent artery occlusion could be predicted and therefore no unexpected neurological deficits or complications were detected in these patients following the procedure. In 1 patient, millimetric MAs requiring parent artery occlusion in 3 distinct distal branches of the left MCA were not treated endovascularly due their fusiform structure and the substantial risk of neurological deficits. These lesions were regressed totally after antibiotherapy in the follow-up DSA examination.

Embolization using coils or liquid embolization agents (Onyx, NBCA, or others) account for the majority of endovascular procedures for the treatment of MAs.⁸ Due to the need for antiplatelet therapy, flow-diverting stents are not preferred for the stabilization of MAs prior to cardiac surgery but have been reported in the treatment of MAs secondary to CNS infections such as meningitis.¹⁵ However, there are also limited reports regarding successful intracranial stenting for the treatment of MAs that are refractory to the initial medical treatment.¹⁶⁻¹⁸ In the modern era with advanced endovascular techniques, microsurgical interventions are commonly reserved for patients with a severe mass effect due to intracranial hemorrhage or those who fail EVT.⁹ In our study, aneurysm sac embolization and parent artery occlusion was performed using glue or coils in 12 of 16 MAs that underwent EVT. Remaining 4 aneurysms were treated without parent artery occlusion due to their wide aneurysmal sacs.

A feared complication of endovascular intervention is abscess formation surrounding the coil mass.^{8,19} However, only a case of abscess formation around the coil was reported in the literature and it was treated with surgical decompression and drainage without coil resection.²⁰ Similar to the literature, none of the cases treated with coil embolization in our study group had any sign or imaging finding of an abscess formation surrounding the coil.

Limitations

Our study has several limitations. First of all, our study was carried out on a limited number of patients with a retrospective design. Another limitation of our study was that all patients in the study group were treated via endovascular approach, so it did not include the outcomes regarding other treatment methods, such as standalone antibiotherapy or surgical treatment. However, the data

of the study maintains its importance due to the fact that endovascular approach has been more frequently preferred in the treatment of intracranial MAs in recent years.

Conclusion

Early diagnosis and meticulous individualized treatment are critical for the successful treatment of MA cases. With the advances in endovascular techniques, the tendency toward endovascular approach for treatment of MAs has increased in recent years, and the success of concurrent endovascular treatment has increased with technical developments. Large-scale multicenter studies will be useful to increase the knowledge regarding these rare vascular lesions.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul University Cerrahpaşa, Cerrahpaşa Faculty of Medicine (Approval No: 660643, Date: April 4, 2023).

Informed Consent: Written informed consent was obtained from all participants of this study.

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